Amendments to the Drawings:

Formal drawings are submitted herewith which incorporate the changes required by the Examiner. Approval by the Examiner is respectfully requested.

Attachment: Replacement Figures 1A, 1B and 1C

REMARKS

Claims 1-17 are rejected. Claims 18 and 19 are withdrawn from consideration. Claims 1, 2 and 4 have been amended. Claims 1-17 are presently pending in the application. Favorable reconsideration of the application in view of the following remarks is respectfully requested.

The basis for the amendment of claim 1 is found on pg. 11, line 29 – pg. 12, line 1 ("*As used herein, the term "latent colorant" means a molecule with adsorption and emission characteristics that can be modulated by chemical or physical means. It is preferred that a latent colorant be colorless and not fluoresce.*") and pg. 12, lines 8-11 ("*As used herein, the term "latent colorant" means a molecule of whose adsorption and emission characteristics can be modulated using a chemical or a physical means. It is preferred that a latent colorant is colorless and does not have fluorescence.*") of the specification as originally filed. The basis for the amendment of claim 2 is claim 2 as originally filed. The basis for the amendment of claim 4 is claim 4 as originally filed.

Restriction under 35 USC § 121:

The Examiner has required restriction to one of the following inventions under 35 U.S.C. 121: I. Claims 1-17, drawn to an array of microspheres with latent colorants, classified in class 436, subclass 518, and II. Claims 18 and 19, drawn to a method of identifying biological analytes by reacting microspheres with latent colorants and tagged analytes, classified in class 436, subclass 56, indicating that the inventions are distinct, each from the other, because, in the instant case, the microspheres recited in Group I can be reacted with analytes that do not have emission tags, and thus the use of the microspheres does not require the step of recording signals from the optical emission tags and microspheres comprising dyes that can be developed only in the presence of the analyte of interest are well known in the art, therefore, microspheres recited in Group I would be capable of detecting analytes that do not comprise emission tags.

The Applicant confirms the telephone election of 12/7/05 in which the provisional election was made with traverse to prosecute the invention of Group I, claims 1-17. Claims 18-19 are withdrawn from further consideration, as being drawn to a non-elected invention.

Specification:

The specification has been amended to identify the commonly assigned copending applications to which this pending application relates.

Claim Objections:

The Examiner has objected to Claim 2 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 2 has been amended accordingly.

Rejection of Claim 8 under 35 USC § 112:

Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 is dependent on claim 3. Claim 8 recites that the optical signature can be used to identify a target analyte. However, claim 3 recites that the optical signature can be used to identify the microsphere. It is not clear whether the optical signature can be used to identify the microsphere, the target analyte or both. The Specification does not appear to support the use of an optical signature that is capable of identifying both the microsphere and the target analyte. However, for the purpose of examination, the claim will be interpreted to mean that the optical signature can be used to identify both the microsphere and the target analyte. As stated by the Examiner, claim 3 recites the developed latent colorant can be used to identify a microsphere. The specification also describes that bioactive probes are attached to the surface of the microsphere (pg. 6, lines 17-18, pg. The colorant, that is, the developed latent colorant, can be used to identify a particular microsphere-biological probe combination. (pg. 12, lines 20-23; pg. 21, lines 6-11). The target analyte then reacts with the biological probe, resulting in a latent colorant-microsphere-probe-analyte combination. (pg. 23, lines 3-24, see also Fig. 1A-C). Once the latent colorant is developed, the colorant-microsphere-probe-analyte combination is identifiable; hence, the colorant can be used to identify the target analyte.

Rejection of Claims 1-5, 7-12 and 14-17 Under 35 U.S.C. §102(e):

The Examiner has rejected Claims 1-5, 7-12 and 14-17 under 35 U.S.C. 102(e) as being anticipated by Chee et al. (US 6,429,027 B1), indicating that Chee et al. disclose a two-dimensional array of microspheres immobilized in wells of a substrate, wherein the concentration of the wells on the substrate is at

least 10,000 per cm^2, the size of the microspheres can range between 0.2 to 200 microns, the microspheres bear biological probes in the form of a bioactive agent, the microspheres comprise a unique optical signature capable of identifying the bioactive agent, wherein the optical signature can be in the form of a fluorescent dye 4, and the fluorescence of the dyes is a photo initiated process involving the absorption of a high energy photon and the emission of a lower energy photon. The Examiner further indicates that the reference discloses another embodiment of the invention comprising microspheres with biological probes in the form of identifier binding ligands that bind to the decoder biding ligands of the target analyte, the IBL/DBL interaction can be an interaction involving metal ion-metal ion ligands, the IBL is a molecule that has the ability to change its color or luminescence properties once it binds to the DBL, thus providing a means to identify the target analyte as well as the microsphere.

Chee discloses sensor compositions comprising a composite array of individual arrays, to allow for simultaneous processing of a number of samples. Comprising a substrate with a surface having a plurality of assay locations, each assay location comprising an array location, said array location comprising a plurality of discrete sites; and a population of microspheres comprising at least a first and a second subpopulation, wherein said first subpopulation comprises a first bioactive agent and wherein said second subpopulation comprises a second bioactive agent; wherein said microspheres are distributed in said discrete sites in said array location.

The present invention relates to a microarray comprising a support, on which is disposed a layer of microspheres bearing biological probes, wherein the microspheres comprise at least one material with a non-fluorescent latent color that can be developed and used to identify the microsphere.

A claim is anticipated under 102(e) only if each and every element as set forth in the claim is found, either expressly or inherently, in a single prior art reference. Verdegaal Bros. V. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Chee describes a "a molecule whose color or luminescence properties change in the presence of a selectively-binding DBL."(col. 15, lines 36-38), "a molecule whose color or luminescence properties change in the presence of various solvents." (col. 15, lines 43-46), "a derivative of fluorescein whose

color changes between aqueous and nonpolar solvents." (col. 15, lines 48-50), and "In general, labels fall into three classes: a) isotopic labels, which may be radioactive or heavy isotopes; b) magnetic, electrical, thermal; and c) colored or luminescent dyes; although labels include enzymes and particles such as magnetic particles as well." (col. 19, lines 33-37). Chee describes a colored molecule that changes to a different color or fluoresces. Chee fails to disclose a latent colorant, that is, a molecule which "is colorless and does not have fluorescence", as defined in the present specification. Therefore, Chee fails to anticipate the present claims.

Rejection Of Claims 6 and 13 Under 35 U.S.C. §103(a):

The Examiner has rejected Claim 6 under 35 U.S.C. 103(a) as being unpatentable over Chee et al. in view of Zuk et al. (US 4,256,834), indicating that although Chee et al. does not disclose that the optical signature is developed by the means recited in the claim, Zuk et al. disclose an immunoassay comprising the use of a chemiluminescer that undergoes an enzyme catalyzed redox reaction to produce a detectable signal, making it obvious to utilize a chemiluminescer disclosed by Zuk et al. as the optical signature means for the microspheres disclosed by Chee et al, since the use of such chemiluminescers would be beneficial in assays in which the assay conditions favor chemiluminescence over fluorescence.

Chee discloses sensor compositions comprising a composite array of individual arrays, to allow for simultaneous processing of a number of samples. Comprising a substrate with a surface having a plurality of assay locations, each assay location comprising an array location, said array location comprising a plurality of discrete sites; and a population of microspheres comprising at least a first and a second subpopulation, wherein said first subpopulation comprises a first bioactive agent and wherein said second subpopulation comprises a second bioactive agent; wherein said microspheres are distributed in said discrete sites in said array location.

Zuk discloses novel immunoassays employing discrete particulate reagents for determining an analyte which is a member of a specific binding pair-ligand and homologous receptor. The assay employs as a first reagent, a member of a pair bound to an insoluble particle (particle conjugate); as a second reagent, a label which is part of a signal producing system, bound to a member of the pair (signal label conjugate); and as a third reagent, a signal repressor comprising an

insoluble particle, where the signal repressor is obstructed from interacting with the label of the signal label conjugate, when the signal label conjugate is bound to the particle conjugate. In performing the assay, the analyte, the reagents, and any ancillary materials are combined in an aqueous assay medium and the signal determined as compared to an assay medium having a known amount of analyte. The repressor greatly enhances the sensitivity and accuracy of the immunoassay in repressing the signal produced by labels which are not bound to the particle conjugate, thus substantially limiting the observed signal to label bound to the particle conjugate. The labels which are employed provide a signal which does not differ significantly from when the signal label conjugate is bound to the particle conjugate or is free in the bulk solution. Illustrative labels include chromogens, such as fluorescers, chemiluminescers, and the like. Particular reagents and kits are provided, where the kits have predetermined amounts of the various reagents to substantially optimize the sensitivity of the assay.

The present invention relates to a microarray comprising a support, on which is disposed a layer of microspheres bearing biological probes, wherein the microspheres comprise at least one material with a non-fluorescent latent (colorless) colorant that can be developed to a color and be used to identify the microsphere.

To establish a prima facia case of obviousness, there must be some suggestion or motivation in the reference or in the general knowledge available to one skilled in the art to modify the reference, there must be a reasonable expectation of success, and the prior art reference must teach or suggest all the claim limitations.

Chee describes a colored molecule that changes to a different color or fluoresces. Chee fails to disclose a latent colorant, that is, a molecule which "is colorless and does not have fluorescence", as defined in the present specification. Zuk also fails to disclose a latent, non-fluorescent colorant as presently claimed. In addition, the reference to Chee relates to an array, which allows the analysis for multiple analytes at once. Zuk relates to analysis of single analytes and contains no disclosure relating to the use of multiple analytes in one assay system. Combining Zuk with Chee would reduce the assay of Chee to detecting single analytes, not the multi-analyte system of the unmodified Chee. As neither reference suggests the use of a color-free material that can be switched on to form

a colored material, especially a non-fluorescing compound, the references fail to provide any suggestion to modify to produce the presently claimed invention.

There is also no likelihood of success provided in the references. There is no suggestion to use a non-fluorescing, colorless colorant, which can be developed to form a colored material. The present invention deals with the problem of background noise caused by fluorescence, which lowers or interferes with the detectability of a material producing an optical signal. (pg. 5, line 10). The references fail to deal with this problem, preferring instead to actually use fluorescent materials.

Neither Chee nor Zuk disclose the use of a latent colorant, a developable latent colorant or a non-fluorescing latent colorant as presently claimed.

The present invention also provides a surprising improvement. The present invention provides improved signal detectability, by providing a latent colorant, which would have no signal, and converting it to a colorant, which would have a detectable signal. The detectability is improved, as detection relates to an "on" / "off" or signal / no signal detection scenario, as opposed to a detection system aimed at detecting a shift in a signal. In other words, the present invention relies on the fact that it is easier to detect a color compared to an absence of color, as opposed to a shift in color.

Since Chee and Zuk, alone or in combination, fail to suggest the modification necessary to produce the present claims, fail to provide any likelihood of success and fail to disclose all of the present claim limitations, the Applicants request that the Examiner reconsider and withdraw the rejection.

Rejection Of Claim 13 Under 35 U.S.C. §103(a):

The Examiner has rejected Claim 13 under 35 U.S.C. 103(a) as being unpatentable over Chee et al. in view of Wang (US 4,663,277), indicating that Chee et al. disclose the microarray of claim 13 except for the recital of the immobilization of the microspheres by a gelation process, and Wang discloses an immunoassay for a virus accomplished by utilizing microspheres coated with antiviral antibodies, in which the method of the immunoassay involves immobilizing the microspheres by placing the microspheres in a gel, making it obvious to one of ordinary skill in the art to further immobilize the microspheres disclosed by Chee et al. by means of a gel as taught by Wang so that the

microspheres disclosed by Chee et al. are better secured within the wells of the substrate.

Chee discloses sensor compositions comprising a composite array of individual arrays, to allow for simultaneous processing of a number of samples. Comprising a substrate with a surface having a plurality of assay locations, each assay location comprising an array location, said array location comprising a plurality of discrete sites; and a population of microspheres comprising at least a first and a second subpopulation, wherein said first subpopulation comprises a first bioactive agent and wherein said second subpopulation comprises a second bioactive agent; wherein said microspheres are distributed in said discrete sites in said array location.

Wang relates to the detection and/or the determination of viruses by an immunoassay method, to materials for such method, and to a virus detection kit. Viruses are detected by means of an immunoassay method in which an extended solid phase coated with antiviral antibody is employed to bind and remove virions from a specimen by forming an immuno-complex with antigens of the virions, a mobile solid phase comprising a dispersion of microspheres coated with the antiviral antibody is used to bind the microspheres to antigens associated with the immuno-complex, and the presence of bound microspheres is detected. The detection sensitivity is amplified by the ability to more readily detect the microspheres, which may be dyed or labeled. The extended solid phase advantageously may be in the form of a dipstick which can be easily contacted with the specimen. A virus detection kit provides the extended solid phase and mobile solid phases, each coated with antiviral antibodies.

The present invention relates to a microarray comprising a support, on which is disposed a layer of microspheres bearing biological probes, wherein the microspheres comprise at least one material with a non-fluorescent latent color that can be developed and used to identify the microsphere.

To establish a prima facia case of obviousness, there must be some suggestion or motivation in the reference or in the general knowledge available to one skilled in the art to modify the reference, there must be a reasonable expectation of success, and the prior art reference must teach or suggest all the claim limitations.

Chee describes a colored molecule that changes to a different color or fluoresces. Chee fails to disclose a latent colorant, that is, a molecule which "is colorless and does not have fluorescence", as defined in the present specification. Wang also fails to disclose a latent, non-fluorescent colorant as presently claimed. As neither reference suggests the use of a color-free material that can be switched on to form a colored material, especially a non-fluorescing compound, the references fail to provide any suggestion to modify to produce the presently claimed invention.

There is also no likelihood of success provided in the references. There is no suggestion to use a non-fluorescing, colorless colorant which can be developed to form a colored material. The present invention deals with the problem of background noise caused by fluorescence, which lowers or interferes with the detectability of a material producing an optical signal. (pg. 5, line 10). The references fail to deal with this problem, preferring instead to actually use fluorescent materials. In addition, the present invention utilizes gel to immobilize the microspheres containing latent colorant on the support to improve robustness and reproducibility of the assay. Chee fails to disclose the use of gelatin to immobilize microspheres on a support and fails to disclose problems with agglutination. Wang also fails to disclose the use of gelatin to immobilize microspheres on a support, teaching the use of gelatin to avoid agglutination (col. 9, line 57). Neither reference provides any reason to add gelatin to the array of Chee.

Neither Chee nor Wang disclose the use of a latent colorant, a developable latent colorant or a non-fluorescing latent colorant as presently claimed.

The present invention also provides a surprising improvement. The present invention provides improved signal detectability, by providing a latent colorant, which would have no signal, and converting it to a colorant, which would have a detectable signal. The detectability is improved, as detection relates to an "on" / "off" or signal / no signal detection scenario, as opposed to a detection system aimed at detecting a shift in a signal. In other words, the present invention relies on the fact that it is easier to detect a color compared to an absence of color, as opposed to a shift in color.

Since Chee and Wang, alone or in combination, fail to suggest the modification necessary to produce the present claims, fail to provide any likelihood of success and fail to disclose all of the present claim limitations, the Applicants request that the Examiner reconsider and withdraw the rejection.

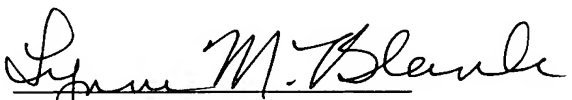
Prior Art:

The Examiner notes that the prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Walt et al. (US 6,023,540) disclose a two-dimensional array of microspheres immobilized in wells disposed at the end of an optical fiber. The microspheres comprise biological probes in the form of functional groups, and a plurality of dyes in varying ratios that define an optical signature for each type of microsphere and ana4yte. The dyes display a change in its optical signature once an analyte exclusively interacts with the functional groups disposed on the surface of the microspheres, which enables one to identify the microsphere and the analyte. However, Walt fails to mention the use of a non-fluorescent, developable, latent colorant.

It is believed that the foregoing is a complete response to the Office Action and that the claims are in condition for allowance. Favorable reconsideration and early passage to issue is therefore earnestly solicited.

Respectfully submitted,



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Enclosures: Replacement Figures 1A, 1B and 1C
Copies of Formal Drawings

If the Examiner is unable to reach the Applicant(s) Attorney at the telephone number provided, the Examiner is requested to communicate with Eastman Kodak Company Patent Operations at (585) 477-4656.